



# ADVANCEMENTS AND DRAWBACKS IN AUTOIMMUNITY: A HOLISTIC REVIEW

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## ABSTRACT

This comprehensive review scrutinizes the progress and challenges in the field of autoimmunity, with a particular focus on the United States. It assesses the intricate roles of immunosuppressive medications, their benefits, and their significant drawbacks, such as increased susceptibility to infections. Emphasizing the need for further research, the paper highlights the criticality of a deeper understanding of the immune system's response to both endogenous and exogenous substances to devise more targeted treatments. Current trends post-COVID-19 and the heightened risks among women due to genetic predispositions are also explored, underscoring the urgency for advancements in autoimmune research.

**KEYWORDS:** Autoimmunity, Immunosuppressive Medications, Immune Response, Autoimmune Research, COVID-19 Complications, Genetic Predisposition

## INTRODUCTION

The Swiss physician Paracelsus stated, "Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided". In order to develop effective medications to treat diseases and infections, we must fully understand the processes of life before introducing any form of medication into the human body. In the case of autoimmunity, there is so much we do not fully understand concerning the immune system, raising concern over existing and future forms of treatment. According to the University of Oxford (2023), the direct causes of autoimmune diseases are unknown when taking into account genetic predispositions and environmental factors, furthering the need for extensive research in the area of study. In order to develop pharmaceuticals that can treat the primary cause of the development of autoimmune diseases, we must first understand what is causing them in the first place. This can only be done through additional research and studies of patients with autoimmune issues. Furthermore, the American Autoimmune Related Diseases Association, a non-profit research organization specializing in autoimmunity, states that "50 million Americans have one or more autoimmune diseases. Approximately 75 percent of those affected are women" (Autoimmune Association, 2019). It is apparent that autoimmunity is negatively impacting the health of millions of Americans, and women are at a higher risk of contracting these complications. Fariha Angnum, a researcher of Internal Medicine from Xavier University, concluded that since large numbers of mutations can occur on the X chromosome in females, they have a greater chance of developing an autoimmune disorder since they are born with two and males only have one (Angnum et al., 2020). It is important to note that the aftermath of the COVID-19 pandemic has left an autoimmune population at large. Research conducted by Kuan Peng from the University of Hong Kong suggests that infection with the SARS-CoV-2

virus could trigger autoimmune responses. He also found that patients who contracted COVID-19 were more likely to develop autoimmune diseases such as rheumatoid arthritis, psoriasis, and multiple sclerosis (Peng et al., 2023). Clearly, COVID-19 has had a significant role to play in the development of autoimmune diseases. One way to treat the symptoms caused by these disorders is to use immunosuppressive medications, which is one of the main forms of treatment. While they are beneficial, they have numerous side effects that can severely weaken the immunity of patients who use them, leading to a higher susceptibility to bacterial and viral infections, as well as other complications. Therefore, immunosuppressive medications have a significant negative impact on a patient's immune system; additional research must be conducted in immunology in order to develop agents that target a specific immune response.

## MATERIALS & METHODS

In-depth qualitative secondary research was conducted to develop new forms of immunosuppressive therapies and medication to alleviate the symptoms caused by autoimmune diseases. This paper aims to effectively analyze and spread awareness of the various complications these forms of treatment may cause in patients.

## LITERATURE REVIEW

An extensive examination of autoimmune diseases and immunosuppressive medications was conducted, utilizing a breadth of resources from the National Library of Medicine. A meta-analysis of these sources was performed to ascertain both the progress and limitations associated with immunosuppressive treatments within the United States populace. The findings indicate a pressing need for further investigation into autoimmunity, particularly in understanding the immune system's response to exogenous substances. This knowledge

is crucial for the development of targeted therapies and pharmaceutical interventions that can address the fundamental causes of autoimmune disorders.

### Role of Immunosuppressive Medications

In order to understand the consequences immunosuppressive medications may have on the human body, we must first analyze their role in the immune system. Yasseen Hussain and Haroon Khan, autoimmunity researchers from Soochow University and Wali Khan University, respectively, define an immunosuppressant as a type of medication used to inhibit or decrease the intensity of an immune response (Hussain et al., 2022). An immune response could be caused by a foreign antigen entering the body or by any type of bacterial or viral infection. When the body recognizes the substance as a foreign entity, it releases antibodies to neutralize it. The immune system also utilizes B cells and T cells, which work together to eradicate any infections in the body. B cells are responsible for the release of antibodies, and they also identify the antigens to be destroyed by the T cells. It is important to note that the development of these medications led to “a greater understanding of the immune response and the study of immune deficiencies and autoimmune diseases,” according to Dr. Alexander Wiseman, a nephrologist who has also conducted research in autoimmunity relating to kidney failure (Wiseman, 2015). Immunosuppressive medications have not only taught scientists more about the immune system, but they have also led to the development of many forms of treatment targeting specific components to inhibit immune responses. Many consist of T and B cell directed therapy, where the main objective is to inhibit regulatory signaling between the cell and the antigen. Another example would be the inhibition of cytokines, signal proteins that manage inflammation. While immunosuppressive medications may seem promising, there are various complications they have the potential to cause that must be addressed.

### Susceptibility to Foreign Infection

Immunosuppressive agents put a patient's immunity at risk for a variety of infections. The primary goal of these drugs is to suppress the immune system's ability to function because they destroy tissues and organs in the body. However, if the immune system grows dramatically weaker due to these agents, it cannot perform its intended function. According to Richard Ruiz and Allan Kirk, the latter being a professor of immunology and pediatrics, a “complication of immunosuppressive therapy is the development of post transplantation infections. The vast majority of infections occur within the first 6 months after transplantation, when the intensity of immunosuppression is at its highest” (Ruiz & Kirk, 2015). Within the first 6 months where a patient is receiving immunosuppressive therapy is their highest chance of contracting bacterial or viral infections. If these types of therapies are used, we may be causing additional medical complications, even though the intention is to treat the symptoms of the autoimmune disease. This is an important issue that must be addressed because the health and safety of patients afflicted with autoimmune diseases are jeopardized. Furthermore, research shows immunosuppressant agents targeting chemokines, proteins that stimulate the migration

of white blood cells in the body, are very difficult to develop. Wiseman adds that there are many “difficulties in successful drug development that can be attributed to poorly predictive preclinical models and an incomplete understanding of those up- or down-regulating chemokines” (Wiseman, 2015). There is a fundamental lack of understanding about how immunosuppressive agents can cause or inhibit a physiological response in the body, specifically in the case of chemokines. Therefore, it is important to consider the side effects these agents may cause when introducing them into the immune system.

### Need for Additional Research

It is critical that additional research be conducted in order to develop treatments that specifically target the autoimmune disease, not just its effects or symptoms on the human body. Ruiz & Kirk (2015) state that “knowledge and understanding of the long-term side effects of immunosuppression can lead to the early detection and treatment of potential complications” (Ruiz & Kirk, 2015). However, the only way to advance the current knowledge of immunosuppressive agents' role in the immune system and the long-term impacts they may have is through scientific research. Hauke Thomsen, a professor in biostatistics and epidemiology, found in his study of about 770 thousand participants a high association between autoimmune hepatitis and other autoimmune disorders (Thomsen et al., 2020). In other words, patients who were diagnosed with autoimmune hepatitis were more likely to develop other autoimmune diseases. These risks were also observed by Thomsen et al. (2020) in families, between siblings, and between spouses. Marta Gonzalez, MD, a researcher specializing in internal medicine, also found a similar result in her study of uveitis. She found a causational relationship between self-reported uveitis and other autoimmune diseases in a study of 5106 Americans between the ages of 20 and 69 (González et al., 2018).

### CONCLUSION

Autoimmunity is an important issue. 800 million people are affected by some type of autoimmune disease across the globe. In order to develop effective therapies and pharmaceuticals to treat the main cause of these conditions, additional research must be conducted in regards to the immune system. Additional insight on its functions and its ability to recognize foreign or self-made substances would be extremely beneficial for the production of new medications to eliminate autoimmune diseases worldwide.

### REFERENCES

1. Angum, F., Khan, T., Kaler, J., Siddiqui, L., & Hussain, A. (2020, May 13). The prevalence of autoimmune disorders in women: A narrative review. *Cureus*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7292717/#:~:text=The%20larger%20number%20of%20genes,whereas%20men%20possess%20only%20one>
2. Autoimmune Association. (n.d.). The american autoimmune 1 every5. <https://autoimmune.org/wp-content/uploads/2019/12/1-in-5-Brochure.pdf>
3. González, M. M., Solano, M. M., Porco, T. C., Oldenburg, C. E., Acharya, N. R., Lin, S. C., & Chan, M. F. (2018, April 17). Epidemiology of uveitis in a US population-based study. *Journal of ophthalmic inflammation and infection*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6000000/>

- nih.gov/pmc/articles/PMC5904090/#:~:text=From%20the%205106%20interviewed%20US,20%20to%2069%20years%20old
4. Hussain, Y., & Khan, H. (2022, April 8). Immunosuppressive drugs. Encyclopedia of Infection and Immunity. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8987166/>
  5. Peng, K., Li, X., Yang, D., Chan, S., Zhou, J., Wan, E., Chui, C., Lai, F., Wong, C., Chan, E., Leung, W., Lau, C., & Wong, I. (2023, August 16). Risk of autoimmune diseases following COVID-19 and the potential ... [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(23\)00331-0/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(23)00331-0/fulltext)
  6. Ruiz, R., & Kirk, A. D. (2015). Long-term toxicity of immunosuppressive therapy. Transplantation of the Liver. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7152453/>
  7. Thomsen, H., Li, X., Sundquist, K., Sundquist, J., Försti, A., & Hemminki, K. (2020, October 20). Familial associations between autoimmune hepatitis and primary biliary cholangitis and other autoimmune diseases. PloS one. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7575086/#:~:text=For%20AH%20only%20the%20risk,one%20couple%20shared%20the%20risk>
  8. University of Oxford. (2023, May 6). Autoimmune disorders found to affect around one in ten people. University of Oxford. <https://www.ox.ac.uk/news/2023-05-06-autoimmune-disorders-found-affect-around-one-ten-people#:~:text=A%20new%20population%2Dbased%20study,about%20one%20in%20ten%20individuals>
  9. Wiseman, A. C. (2015, July 13). Immunosuppressive medications. Clinical journal of the American Society of Nephrology : CJASN. <https://pubmed.ncbi.nlm.nih.gov/26170177/>